National Aeronautics and Space Administration

Ames

Discovery Innovations Solutions

NASA Laboratory Analysis for Manned Exploration Missions

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Sensing Technologies for Global Health, Military Medicine, and Environmental Monitoring IV
Paper #: 9112-67

Overview

- Background
- Mission Operations
- Requirements
- Technology Development
- Summary

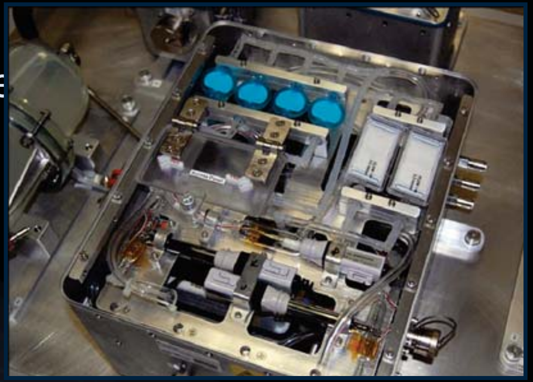
Organization

- **Human Research Program**
  - Behavioral Health & Performance
  - Human Health Counter-measures
  - Space Human Factors & Habitability
  - Space Radiation
  - Exploration Medical Capability (ExMC)
  - ISS Medical Project

- The Human Research Program is divided into 6 major elements:
  - Provide the Program's knowledge and capabilities to conduct research, addressing the human health and performance risks
  - Advance the readiness levels of technology and countermeasures to the point of transfer to the customer programs and organizations
- The National Space Biomedical Research Institute (NSBRI) is a partner with the HRP in developing a successful research program.

Exploration Medical Capability Element

- The Exploration Medical Capability (ExMC) Element is charged with: Reducing the risk of unacceptable health and mission outcomes due to limitations of in-flight medical capabilities for exploration missions.
- To reduce this risk, ExMC
  - Defines requirements for health maintenance
  - Develops treatment protocols
  - Extrapolates from the protocols to health management modalities
  - Evaluates the feasibility of these modalities
  - Develops technology and informatics that will enable medical care and decision systems
  - Utilizes ground, analog, and flight resources



Intravenous Fluid Generation (IVGEN) Assembly that Purifies Water Coming from the Space Vehicle

Exploration Medical Care

Objective: Ensure astronaut health and safety due to injury or illness on extended (>30 days) human exploration missions beyond LEO - Level IV & V standards of care.

TABLE 3.5.5.3.5-1 MEDICAL CARE CAPABILITIES

Level of Care	Mission	Capability
I	LEO < 8 days	Space Motion Sickness, Basic Life Support, First Aid, Private Audio, Anaphylaxis Response
II	LEO < 30 days	Level I + Clinical Diagnostics, Ambulatory Care, Private Video, Private Telemedicine
III	Beyond LEO < 30 day	Level II + Limited Advanced Life Support, Trauma Care, Limited Dental Care
IV	Lunar > 30 day	Level III + Medical Imaging, Sustainable Advanced Life Support, Limited Surgical, Dental Care
V	Mars Expedition	Level IV Autonomous Advanced Life Support and Ambulatory Care, Basic Surgical Care

LEO – Low-Earth Orbit

Ref: NASA CxP 70024 – Constellation Program Human-Systems Integration Requirements (Revision B), March 3, 2008.

Ref: NASA-STD-3001, Volume 1, NASA SPACE FLIGHT HUMAN SYSTEM STANDARD VOLUME 1: CREW HEALTH, Approved: 03-05-2007.

Currently Available for Spaceflight

- International Space Station (ISS) medical diagnostics capability maintains very limited capability for in-flight analysis of bodily fluids (urine, blood, saliva).
- Upmass availability for re-supply
- Two diagnostic instruments are onboard the ISS
  - Portable Clinical Blood Analyzer (PCBA) or i-STAT (Abbott) provided by United States
  - Reflotron (Roche) provided by Russians
- Though some in-situ diagnostic capability demonstrated, several drawbacks for space exploration persist
  - Refrigerated disposables; limited shelf-life
  - Unable to provide blood cell analysis
  - Waste/consumables

ISS i-STAT PCBA

Ref: http://www.nasa.gov/mission_pages/station/research/experiments/373.html#images

Exploration Laboratory Analysis (ELA)

ExMC Gap 4.05*

– *We do not have the capability to measure laboratory analytes in a minimally invasive manner during exploration missions.*

To address this gap, an exploration lab analysis platform technology for long-duration, exploration missions should:

- Be minimally invasive
- Be easy to use
- Promote crew autonomy
- Exhibit expanded assay capability
- Have extended shelf-life of consumables (e.g. reagents, cartridges)
- Minimize mass, volume, power, and consumables

**https://humanresearchwiki.jsc.nasa.gov*

ELA Operational Concept

User
- Crewmember
  - Sample acquisition
  - Sample preparation

Hardware
- Sample Analysis
  - Analyzer 1
  - Analyzer 2

Data Manage-ment
- Integral to hardware
- Data processing, storage, transmission
- Wired/wireless communication to PC

EMS
- Wired/wireless integration hardware
- Medical diagnosis, evaluation
- Ground support

EMS –
Exploration Medical System

ELA Performance Considerations

Performance Consideration	Value	Comment
Shelf life, durables and consumables	36 months	Storage under the exploration vehicle's ambient environment conditions; no refrigeration
Operational life in space	36 months	Survive possible high-energy and background radiation exposure
Reliable usage time	144 hours	Battery power operability
Gravitational/residual acceleration	1, 0.38, 0.17, 10^{-5} g	Must operate on Earth, moon, near-Earth asteroid, Mars, and in low-Earth orbit
Consumables volume (includes reagents and disposables)	TBD (cm^3)	Depends on medical kit dimensions
Mass	TBD (kg)	Depends on medical kit dimensions
Power consumption	TBD (W)	Battery operation; vehicle back-up
Volume	TBD (cm^3)	Depends on medical kit dimensions

ELA Functional Requirements

MEASUREMENT PANELS

Basic Metabolic	Blood Gases	Hematology	Cardiac	Liver	Urinalysis
Glucose	PaO_2	WBC Count	Troponin I	Total Bilirubin	Specific Gravity
Calcium	$PaCO_2$	RBC Count	CK-MB	Direct Bilirubin	pH
Sodium	SaO_2	HCT		ALP	Leukocytes
Potassium	HCO_3	Hgb		AST	Nitrites
CO_2, Total	pH	Neutrophils		ALT	Proteins
Chloride		Abs. Neutrophils Count			Glucose
BUN		Lymphocytes			Ketones
Creatinine		Monocytes			Urobilirubin
		Eosinophils			Bilirubin
		PLT			Blood
					Urate

Ref: Exploration Medical Capability Functional Requirements Document, Baseline, March 2011, NASA JSC-65982.

NASA SBIR Technologies

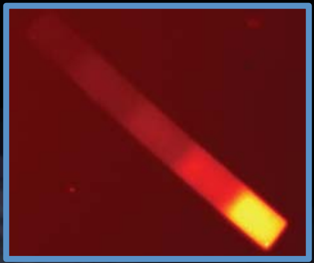
Solicitation/Subtopic/Title:

- NASA SBIR 2007 solicitation, Exploration Medical Capability
  - Reusable Handheld Electrolytes and Lab Technology for Humans (rHEALTH Sensor), DNA Medical Institute
- NASA SBIR 2008 solicitation, In Flight Diagnosis and Treatment
  - Nanoscale Test Strips for Multiplexed Blood Analysis, DNA Medicine Institute
- NASA SBIR 2011 solicitation, Smart Phone Driven Blood-Based Diagnostics
  - Cell Phone-based Lateral Flow Assay for Blood Biomarker Detection, Intelligent Optical Systems, Inc./Holomic

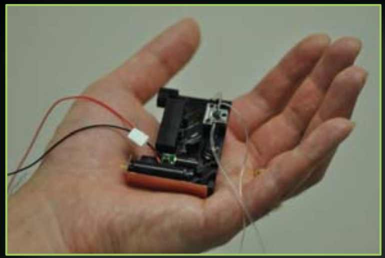
rHEALTH Technology

Spiral Vortexer

Capillary Collector, Saline/Waste



Nanostrips



Optical Block

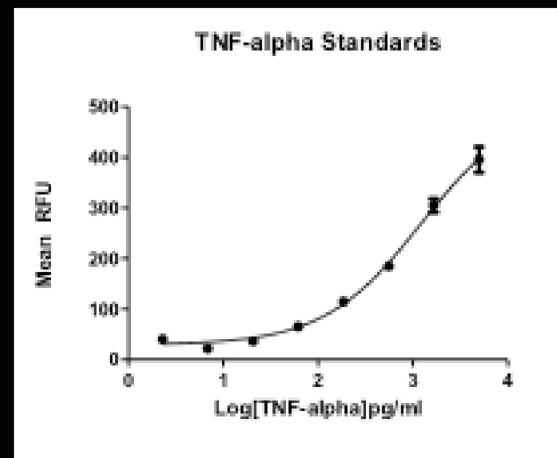
Courtesy of The DNA Medicine Institute

rHEALTH Capabilities

One drop = 100s of tests

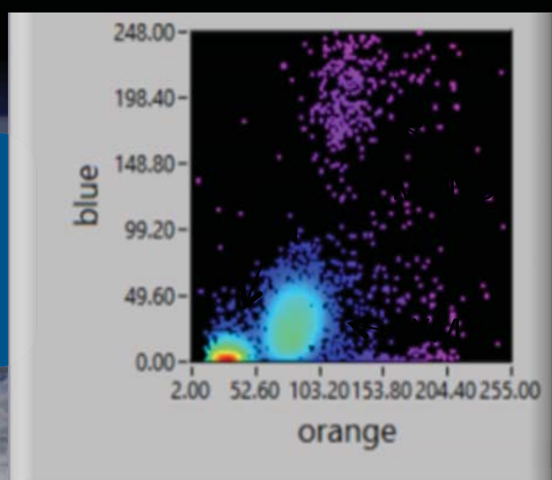
Courtesy of The DNA Medicine Institute

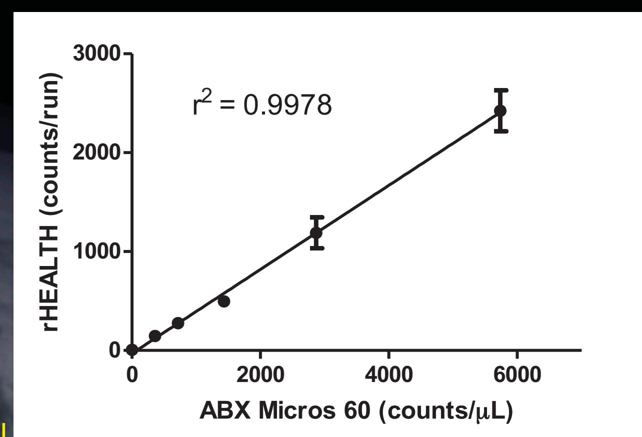
5 – 10 µL sample volume



Multiplexed Immunodx

Cell subtypes



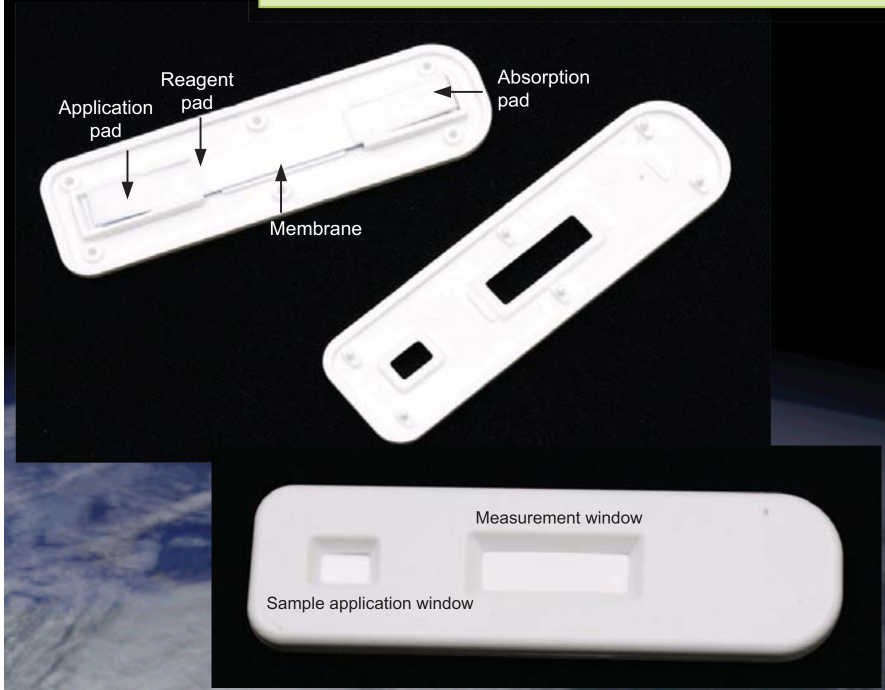


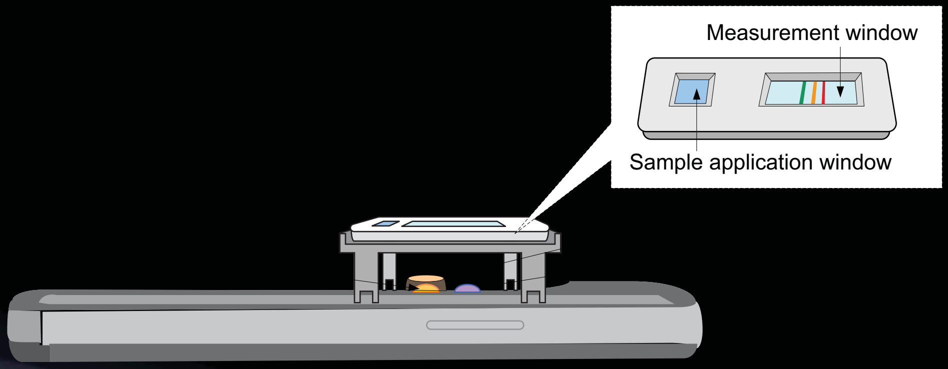
Cell counting

Smartphone Diagnostics – IOS Lateral Flow Assays (LFA)

Concept – develop a simple and compact point-of-care platform

- Integrate lateral flow test strip with cell phone
- Demonstrate blood biomarker detection
- Perform diagnostics in absence of medically trained personnel





Cell phone with LFTS cassette holder attachment, modified for fluorescence imaging

Courtesy of Intelligent Optical Systems (IOS)

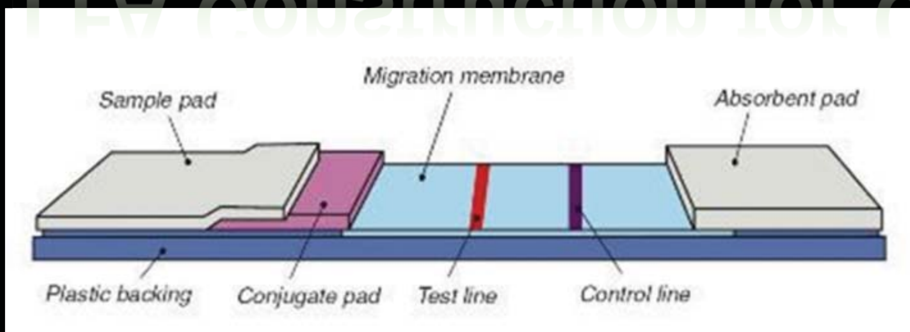
Advantages of Smartphone Diagnostics

- Over 5 billion cellphone subscribers worldwide
  - Commodity; less expensive than fabricating a reader(s) for multiple assay configurations (i.e. immunoassays, electrochemical assays, hematology)
- Telemedicine - remote, biomedical diagnostic applications
  - Leverage development of apps and assays
  - Standardized reconfigurable user interface, communication, data processing and data storage platform.
- Highly compact analyzer, including attachments
- Cellphones in-use on ISS and Small Satellites – *space ready*
- *Potential basis for future personalized medicine and decentralized healthcare; <u>need for lower healthcare costs</u>*

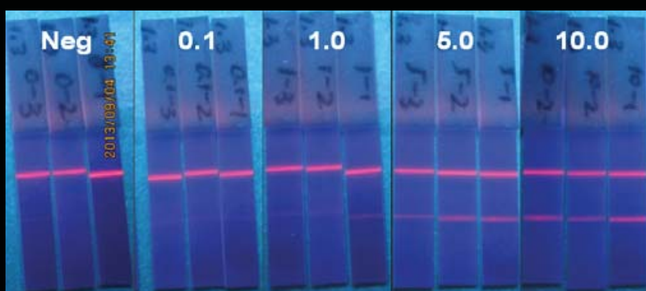
Smartphone Diagnostics Development

Institution	Laboratory	Cellphone Application	Citation
Harvard	Whitesides	Paper microfluidics	Martinez, et al, (2008) Anal Chem 80: 3699–3707.
UC Berkeley	Fletcher	Microscope	Breslauer, et al., (2009) PLoS ONE 4:e6320.
UCLA	Ozcan	Lens-free microscopy	Tseng, et al., (2010) Lab Chip 10: 1787–1792.
UC Davis	Washmann-Hogiu	Microscope/ spectrometer	Smith, et al., (2011) PLoS One 6: e17150.
U. Cincinnati	Papautsky	Colorimetric strip test reader	Shen, et al., (2012) Lab Chip 12: 4240–4243.
U. Arizona	Yoon	Lateral flow assay imager	You, et al., (2013) Biosens. Bioelectron. 40: 180–185.
U. Illinois	Cunningham	Photonic crystal spectrometer	Gallegos, et al., (2013) Lab Chip 13: 2124–2132.
Cornell	Erickson	Colorimetric reader	Oncescu, et al., (2013) Lab Chip 13: 3232–3238.

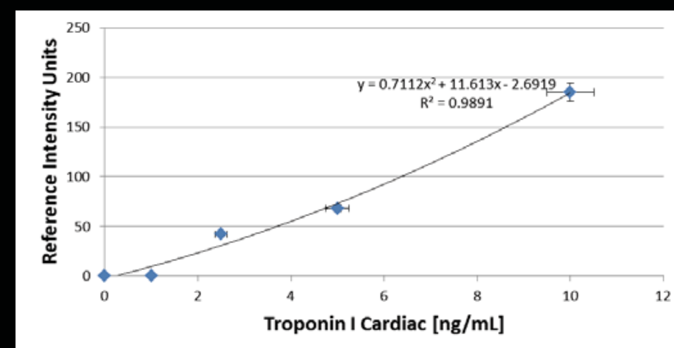
LFA Construction for Cardiac Panel

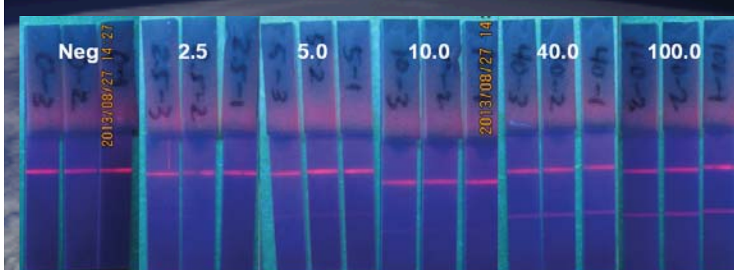


Assay Calibration

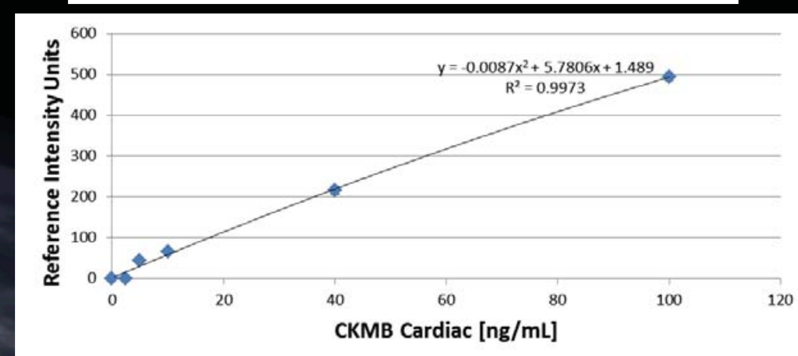


Troponin I [ng/mL]	Peak Height (Avg)
0	0
1.0	0
2.5	42.1
5	68.1
10	185.2



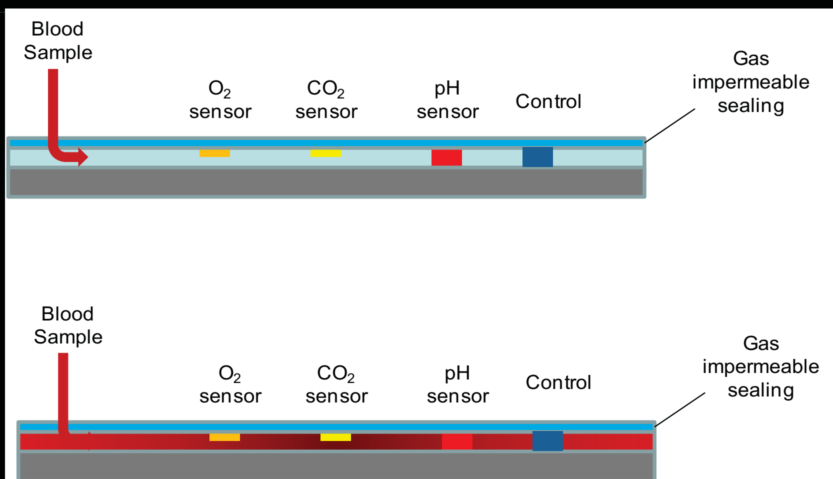


CK-MB [ng/mL]	Peak Height (Avg)
0	0
2.5	0
5	43.8
10	65.4
40	215.1
100	493.2

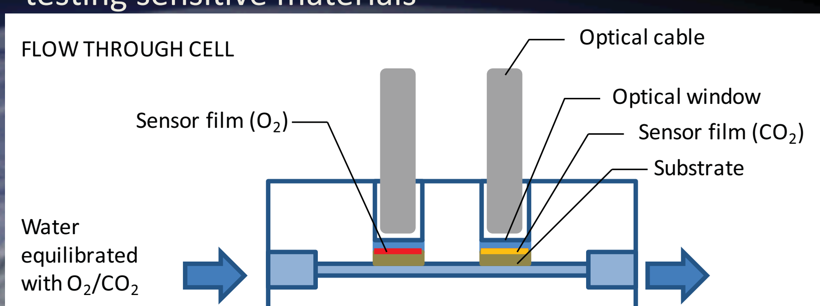


LFA Construction – Dissolved Blood Gas Panel

Design of test strips for blood gas panel analysis

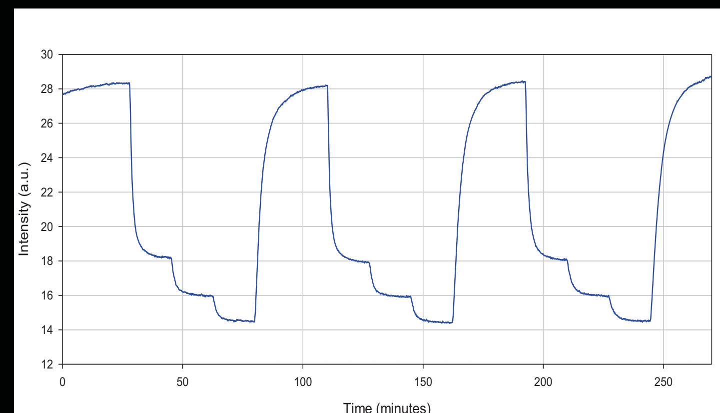


Multi-well flow-through cell for rapidly testing sensitive materials

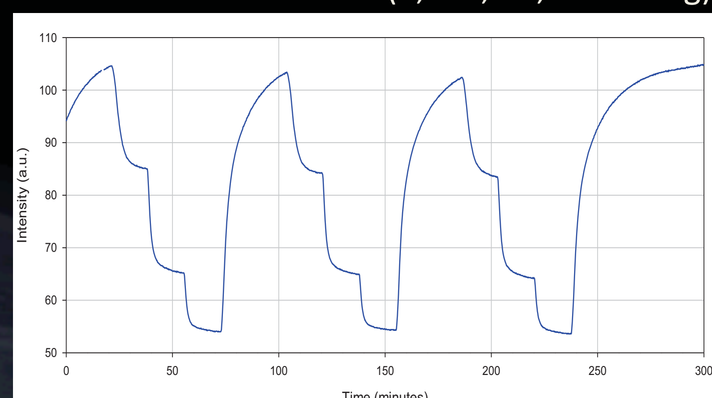


Response Profile of Sensor Materials

Response to dissolved ppO_2 in water (0, 75, 115, 150 mmHg).



Response to dissolved ppCO_2 in water (0, 7.5, 23, 45 mmHg)



Smartphone Diagnostics – Lateral Flow Assay Test Strip Reader

RAPID DIAGNOSTIC TEST (RDT) READER

- ✓ MULTIPLEXED DIGITAL EVALUATION OF LATERAL FLOW TESTS
- ✓ UNIVERSAL AND QUANTITATIVE
- ✓ COST-EFFECTIVE
- ✓ ACCURATE (CV < 2%)
- ✓ SENSITIVE (LIMIT OF DETECTION < 0.5% OD)
- ✓ INTEGRATED INTO THE CLOUD
- ✓ ENABLES SPATIO-TEMPORAT MAPPING OF DISEASES AND CONDITIONS

Courtesy of Holomic, LLC

Holomic Mobile Phone Labs

Courtesy of Holomic, LLC

ELA Timeline

- Select for ground demonstration – 2015
- Select for flight demonstration – 2017
- Ground demonstration – 2018
- Flight demonstration - 2020

Summary

- Space environment and missions present unique challenges for ELA
  - Microgravity (control of bubbles in microfluidics)
  - Minimizing consumables/waste
  - Accommodation by the exploration medical kit (mass, volume)
  - Extended instrument performance throughout lengthy deployments
  - Extended shelf-life
- Possible technological solutions are under investigation
- Path for closing ExMC Gap 4.05 for ELA has been identified